Exhibit C

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

ORIGINAL

SMITH KLINE & FRENCH)
LABORATORIES LIMITED and)Civil Action No.
SMITHKLINE BEECHAM CORPORATION)05-197
d/b/a GLAXOSMITHKLINE,)
Plaintiffs,)
vs.)
TEVA PHARAMCEUTICALS USA, INC.,)
Defendant.)

THIS DEPOSITION TRANSCRIPT CONTAINS CONFIDENTIAL MATERIAL THAT IS SUBJECT TO PROTECTIVE ORDER

Confidential Videotaped Deposition of:

DAVID OWEN

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ENGLAND

May 26, 2006

facilitate technology transfer in the university in Cardiff, which is where the Abcellute and Q-Chip connections come.

Q These companies and organizations that you mentioned having executive or director positions with, do those companies -- do any of those companies have relationship with GlaxoSmithkline?

MS. WIGMORE: Objection to form.

A Does that mean --

MS. WIGMORE: You can go ahead and answer.

A Okay, because one of those companies, Abcellute, has made a small number of sales to GlaxoSmithkline.

Q What does Abcellute sell?

A Abcellute sells preserved hepatocytes.

Q Okay, so just to round out this area, do you have any current relationship with GlaxoSmithkline other than your work on this litigation?

A No.

Q You previously mentioned US patent 4824860, it's been marked in a previous deposition

as exhibit 17, and I'll give you a copy now. (Handed).

A Okay.

Q Do you recognize that document, Dr. Owen?

A Yes, I do recognize it.

Q When was the last time you saw it?

MS. WIGMORE: I'm going to object and instruct you not to reveal the substance of any communications you may have had with lawyers. If you can answer otherwise, go ahead.

A Would you repeat what you just advised me?

MS. WIGMORE: I'm instructing you not to reveal the communications you may have had with any attorneys. If you can otherwise answer that question, go ahead.

A With the exception of the interaction with attorneys, I suspect I last saw it around about the time it was prepared.

Q Okay. Can you tell me how the application for this patent was prepared?

A How it was prepared?

Q For example, who prepared it, and what

your involvement was with it.

A Who prepared it is the patent department, at what was then SmithKline & French. How did they prepare it? They prepared it according to their own professional expertise after discussions with me and no doubt with others, but I --

Q You said that the patent department prepared it. Were there any specific individuals that you know of that prepared the patent application?

A I don't know who prepared the application as it's presented to you here. My recall of the interaction with the patent department was predominantly an interaction with Peter Giddings, but what went on beyond that within the patent department is not known to me and I suspect was never known to me.

Q You mentioned that you spoke with someone in the patent department and it was likely Peter Giddings, is that accurate?

A I think it's probably prudent, with the passage of time, to put likely, but I think

to speaking with your attorneys, you reviewed this patent. Did you review the United Kingdom patent application?

A Wait a minute, when did I --

Q Prior to speaking with your attorneys, I asked you when was the last time you looked at it.

A And I told you I imagined it was 1989.

Q Okay, so when the patent issued?

A And that's because -- well, I'm concerned I may be speculating, but it seems sense to me that I must have done at that stage, because I don't recall it. A lot of things happened in a lot of times, as I'm sure you understand.

Q Do you remember if you reviewed the United Kingdom patent application that's referenced on the cover page of the 860 patent before it was filed?

A I don't absolutely remember, no.

Q Do you remember if you reviewed the US patent application from which the 860 patent issued before that US application was filed?

A I don't remember it as an absolute fact.

Q Can you tell me how the invention that's described in this 860 patent was conceived?

MS. WIGMORE: I'm going to object to the extent it calls for a legal conclusion, you can give your own understanding.

A I'll explain to you what I remember that I did. Ropinirole, under its company number, was the subject of research activities in the SmithKline research site in Upper Merion, and on the basis of the data that was available at that point, was designated for development as a cardiovascular drug. At a point, and I don't know the substance and the facts of it, a decision was made by the top management in Philadelphia that the relative research -- the relative resources for preclinical research were unduly stretched in Philadelphia, but there was capacity to do the preclinical development work of this compound in the UK. So a transfer was made.

I was a senior member of the UK R&D team in the UK, and I felt it was important, if we were to try and do justice to this drug, that we

looked at whatever information was available to us at this time, but also conducted some studies ourselves for the purpose of understanding the compound. If I could give that a context --

Q Let me ask you a little bit about the context, not to interrupt, but you mentioned that the project was transferred from Philadelphia to the UK.

A Yes.

Q Were you involved in the project while it was being worked on in Philadelphia?

A I was not in any way directly involved in the project, and I use the word "directly" deliberately, because there was increasing exchange across the Atlantic at this time, and so people from Philadelphia may well have attended reviews of the research programs that were taking place in the UK, and people like myself would occasionally go to the research reviews that were taking place in programs in Philadelphia.

I certainly went to some program reviews in Philadelphia. I've thought hard and long

speculation.

A I don't know.

Q After the project, the ropinirole project was transferred to the UK, were people in Philadelphia still involved?

A I don't really know what people in Philadelphia were doing. In a nonresearch sense, for example, these -- management of these project teams would have somebody from the marketing department, and I certainly recall a guy called Al Strack was marketing guy from Philadelphia, who would go to virtually all these meetings, he was a kind of permanent guy on an airplane. But substantively from R&D, I really don't know -- I don't remember is a more accurate way to express it. You were asking me what I was -- do you want me -- or do you not want me to continue? I don't know.

Q Let me just make sure that I -- before I ask you to continue about that. So you mentioned that the project was transferred to the UK, is that the point at which you first became directly

involved in the development of ropinirole?

A Yes.

Q So what did you -- so I had interrupted you from answering what you did to conceive of the invention described in the 860 patent.

MS. WIGMORE: My same objection stands, but go ahead and give your understanding.

A Sorry, I'm getting confused between what the two of you said now, I'm trying hard to listen. What did you -- sorry, could I ask you what you asked me again, please?

Q I was just asking you to continue your answer to the question of what you did to conceive of the invention described in the 860 patent.

MS. WIGMORE: And I had objected to the extent it calls for a legal conclusion, but you can give your answer.

A I can say what I did, can't I, without running foul of that? Can I spend one more moment to give it a context? I was the senior pharmacologist in the UK and responsible for a significant number of laboratories; I've been

trying to work out who was when, and the chronology's not easy, but I was responsible for a number of laboratories, in one of which we were doing the pharmacology for an antihypertensive program, so in terms of that, we also regarded ourselves -- and all those programs had, as part of their nature, that they were cardiovascular programs, or they were histamine programs, two types, but what we knew about was also cardiovascular.

When I read the information, I was of the view that there were a small number of studies which I nevertheless always paid particular attention to with our own compounds, which had not been done, and which it was my preference, because I'm not sure there's a right and wrong here, but there is a professional preference, and I was of the view that the -- we would understand the properties of what was then 101468 better if we did some conscious animal cardiovascular measurements, particularly being blood pressure and heart rate, and certainly as part of profiling compounds, we

were of the habit of dosing -- entering into a sort of short-term, but a number of doses, chronic administration, in the sense of administering on a number of occasions to the same animal, and those were studies which had not been done in Philadelphia, they were studies, I guess by preference, rather than right or wrong, that we in the UK preferred to have done.

Roger Eden was the head of one of my laboratories, and it was in his laboratory that a particular type of experiment was done, at my direction, and Annette Wright was the person who actually did the day-to-day experiments. So we initiated experiments of the sort with which we were familiar from our own programs, and started some of these conscious animal cardiovascular studies with 101468.

Q Let me see if I can clarify something. You mentioned two different types of tests, I believe, one is conscious animal studies and then the second, I believe, was short-term testing with a number of --

extent it would require you to reveal the substance of any attorney-client communications. If you have knowledge otherwise, go ahead and answer.

A I know of them only as a result of what I learned during preparation.

Q So at the time you were actually doing your research regarding ropinirole, you weren't aware of any noncardiovascular conscious animal studies that had already been conducted before the start of your work on the project?

A The way I'd like to answer that is by saying what I was aware of was that this was a compound with cardiovascular activity, and the information was that it had no CNS effects. That's not -- you understand why I've answered it in that way.

Q You said that it had no CNS effects, was that something that you learned when the ropinirole project was moved to the UK?

A It must have been.

Q Did you do testing on the CNS effects of

ropinirole?

A Not initially. We did -- it was a cardiovascular drug. We, I was, my labs were cardiovascular people. We did the experiments that we thought were appropriate to extend our understanding of the cardiovascular profile, that was the purpose, that's what we do, that's what we know about.

Q Okay. At some point, was testing on the CNS effects of ropinirole conducted in the UK?

MS. WIGMORE: Objection.

A Studies on the CNS effects of ropinirole were made in the UK, yes.

Q Why were those studies done?

A Well, I'd like to bring that back into context, if I might, please.

Q Sure.

A You asked me initially what we'd done, and we, if you will, have moved on before we've had that answer.

MS. WIGMORE: I just want to be clear in making an objection. He was asked to explain

the conception, I don't think we've gotten through that story, and you now seem to be asking different questions so perhaps if we could have an answer to that question, the record will be more clear.

MR. BRAHMA: We'll tie back to that in a moment.

MS. WIGMORE: I just want to make sure we do get back because he's only finished part of his answer.

A So we undertook cardiovascular studies, that was to say cardiovascular studies were undertaken by people who reported to me, in labs for which I was responsible, cardiovascular studies in conscious animals. As a consequence of doing those studies, and because of the behavioral responses in the animals, the agitation and the signs of -- a word I find very hard to pronounce, but stereotypy, we had cause to believe the compound may well have CNS activities, that is the most -- even to somebody who is first and foremost and predominantly a cardiovascular pharmacology, that is

the most obvious conclusion for those phenomena, so what happened is kind of where all this questioning started, is that under my instruction, Annette Wright, working in Roger Eden's laboratory, did these studies --

Q When you say did these studies, do you mean the cardiovascular studies?

A She did the cardiovascular studies, yes, I thought that's what we were still talking about. They were studies of a nature that she would do most days, and she observed that clearly there were some behavior change in the rats with which she was not normally familiar, and she came to my office to ask me if I was free to come and look at the rats, which is what I did, at which point it seemed to me evidence that the most probable interpretation of behavior was that there were indeed CNS activities of the compound.

What I should say to you is my initial reaction was one of concern, because we were being asked to continue the development of a cardiovascular drug without CNS effects which had

come from my colleagues in Philadelphia, and as a general rule, you would not really wish to see CNS effects at the sorts of doses which you use to lower blood pressure.

Q Just so the record's clear, when you say CNS, you mean central nervous system?

A Yes, I do. So as a -- certainly not immediately, because my first concern was, oh dear, there's a problem here, and we're going to be seen as the guys creating the problem; on the other hand, an adage which I had been taught is as long as you do proper studies, the compound is what the compound is in your results, I formed the view that actually, this may actually be an advantage, rather than a problem, and that we may have a drug which would be useful for the treatment of Parkinson's disease. So over a short period of time, and I can't be precise what I mean by that, but not very long, but definitely not instantaneously, I conceived the hypothesis that this may be a treatment for Parkinson's disease.

Q And would it be fair to say then that you

came to that hypothesis, that ropinirole could be used for the treatment of Parkinson's disease, based on the observation of stereotypy and agitation in the rats that Annette Wright was working with?

A Yes.

Q Was there anything else that you based that hypothesis on?

A I think I have to include -- remember at this point I was the senior pharmacologist in the UK, I guess at that stage I would have been seen as one of the senior pharmacologists in the country, you know, I was a member of the editorial board of the British Journal of Pharmacology, I would go to the meetings of the Pharmacological Society, on occasions I would chair sessions, so I was a cardiovascular guy plus some histamine knowledge, because of the nature of Smith Kline and Tagamet, etcetera, and I went to a lot of meetings. The totality of what was in my mind at that stage to conceive what was my hypothesis I can't be sure about, it's a lot of general knowledge and some specific things.

Q But as far as the specific data related to ropinirole, was that the only data you considered before coming to your hypothesis that ropinirole could be used to treat Parkinson's disease?

MS. WIGMORE: Objection.

A I can't -- it's too long ago for me to be precise about everything which would have passed through my mind at that stage, I just cannot recall that level of detail. I would say absolutely that the evidence that there were -- that there was agitation and stereotypy in the rats would have been a factor, beyond a doubt, probably a rather large factor.

Q So let me back up a step. You said that when the ropinirole project was transferred to the UK, you had received information from the Philadelphia group indicating that ropinirole had no CNS effects, is that correct?

A No, I told you I cannot recall the detail of exactly what I was told, what was contained in the reports from Philadelphia. You're testing my memory beyond the point I can recall. I also told

otherwise, go ahead.

Q I'm willing to let you talk.

A I know, they told me that you would be. I can't recall how I did that.

Q How you did what?

A How I first communicated to others that we had seen these effects which we were interpreting as central nervous system effects. I don't recall how that was.

Q Do you remember when you first communicated to anyone else your hypothesis that ropinirole could be used for treating Parkinson's disease?

A The best recall I have was that I telephoned Professor Costall in Bradford. If you're asking me, did I talk to colleagues prior to that, and I'm not sure which you were asking me, so perhaps I should have asked you, but I can't recall who else I might have spoken to. I was of sufficient seniority that I could make decisions of that nature without having to run to anybody else; equally, I was responsible for my decisions.

properties of clonidine, which was at one time an interesting compound, indeed it made it to the market for a while, but it's not a terribly good antihypertensive agent. It acts through its effects within the central nervous system to elicit peripheral cardiovascular effects. So we worked on that project. I brought to the project the cardiovascular activities, and Lionel Finch brought to the project the CNS effects.

Q Did Dr. Finch have experience in testing compounds for anti-Parkinson's effectiveness?

MS. WIGMORE: Objection.

A Not to my knowledge, and I think I would know if he did.

Q Okay. You previously said that Professors Costall and Naylor had both a reputation for working in the area of anti-Parkinson's research and also I believe you said the proper models for doing that testing.

A They had developed models in order to study anti-Parkinson's activities, yes.

Q What models had they developed?

A The principal one known to me was their marmoset model.

Q And that was known to you before you approached Professors Costall and Naylor?

A I knew they had that, yes.

Q So when you approached Professor -- I guess you first spoke with Professor Costall, correct?

A That's how I recall it, yes.

Q So when you first spoke with Professor Costall, did you direct her to run tests using this marmoset model on ropinirole?

A What I recall asking Brenda Costall, or what I recall telling her was the nature of the hypothesis that I had formed, and that -- gosh, I was going to say I hoped, I'm not quite sure what the right verb is there, but I believed that her expertise would be greater than my expertise in order to confirm the validity of what was my hypothesis, and clearly, I went to her because I believed she had expertise that I didn't have myself. I was a cardiovascular guy. I was referred

to by my boss as a plumber, which is a fair comment if you think about it, it's about pumps and pipes.

Q So prior to approaching Dr. Costall to do this experimental work, did you have a definite idea that ropinirole could be used to treat Parkinson's, or was that more of a guess?

MS. WIGMORE: Objection.

A No, it was absolutely in my mind that it could be a treatment for Parkinson's disease, that is a hypothesis that was formed, but I needed others to confirm it, I didn't have the experimental models under my direction to confirm that. I wanted people who if they confirmed it, others would believe them.

Q And why did you believe, prior to approaching Professor Costall, that ropinirole could be used to treat Parkinson's disease?

A We had evidence of a selective dopamine agonist showing evidence that we interpreted as consistent with CNS pharmacology, and now you're asking -- in a sense, if you're asking me to go beyond that, because to me, that provided the basis to believe that it was a sound hypothesis to believe

Gallagher article that we --

A Correct, correct.

MS. WIGMORE: Before you go on, I just want to object to the characterization as his patent. Could you be clear and use 860? I think that would make the record more clear, but go ahead.

Q Is this not your patent, Dr. Owen?

MS. WIGMORE: Objection, calls for a legal conclusion.

A I'm content that it says inventor, David AA Owen, and that is me. I'm not sure whether otherwise hairs are being split.

Q Is there anyone else that you think invented this invention that's described in this 860 patent?

A I understand entirely that inventorship is a legal matter. To the best of my knowledge, and I don't have that legal expertise, nobody else is an inventor.

Q What is your understanding of what the term inventorship means?

MS. WIGMORE: I'm going to object, calls for a legal conclusion. Answer if you're able.

A I'm going to -- I'd like to answer with a context. Although I can't remember the details of everything that was done, it was my nature and my style to be transparent. I disclosed information to the patent department, and in my view, quite correctly, the patent department were the determinants of who was the inventor.

Q So did you disclose to the patent department whether anyone else worked on the development of ropinirole as a treatment for Parkinson's disease?

MS. WIGMORE: I'm going to object and instruct you not to answer.

A I will take my instructions.

Q I'm going to mark as exhibit 97 a declaration that you signed.

(Exhibit Defendants' 97 marked for identification)

A Okay.

Q Do you understand what a declaration is?

A Yes, I believe so.

Q You understand the statements there?

A I understand there were a series of statements which I would have read.

Q If you look on the first page of exhibit 97, if you go to the second paragraph, it says:

"I believe I'm the original first and sole inventor, if only one name is listed below, or an original first and joint inventor, if plural names are listed below, of the subject matter which is claimed and for which a patent is sought on the invention entitled", and then it goes on.

Do you see that?

A I do.

Q At the time you signed this declaration, did you believe that statement to be true?

A Yes, I did.

Q There's only one inventor named on the patent, correct?

A Correct.

Q So am I accurate in understanding that at

the time you signed this declaration, you believed that you were the original first and sole inventor of the invention, or of the subject matter that's claimed in the 860 patent?

A That is what I believed, and the reason I believed it is, as has been said, it's a legal judgment, and that was the advice given to me by the patent department.

MS. WIGMORE: I'm going to instruct you not to reveal the substance of any communications.

Q Did anyone explain to you what the meaning was of the term inventor as used in that sentence?

MS. WIGMORE: I'm going to instruct you not to answer to the extent your answer would require you to reveal the substance of any attorney-client communications.

A I don't recall at this time.

Q So you don't know whether at the time you signed this declaration you knew what the term inventor meant?

MS. WIGMORE: Same instruction.

remember what you gave to anyone in the patent department relating to the preparation or submission of this patent application that led to the 860 patent?

MS. WIGMORE: You can answer that without revealing the substance of any communication.

A I don't remember it anyway. I really don't.

Q Just to make sure the record's clear, is it accurate to say that you don't remember what you gave to anyone in the patent department relating to the preparation of the United Kingdom application from which the 860 patent claims priority?

MS. WIGMORE: Same instruction. When you say what he gave, are you talking about documents?

MR. BRAHMA: Documents or information, could be orally conveyed.

MS. WIGMORE: So you're asking if he remembers anything he shared with them in any way?

MR. BRAHMA: That's right.

MS. WIGMORE: You can answer, but you cannot reveal the substance of any communication.

A I simply don't remember it. It almost seems slightly strange to me that I don't remember it, but I don't remember it, and therefore, I'm simply unable to tell you.

MS. WIGMORE: Can we break for lunch now? It's been quite some time since we began.

MR. BRAHMA: Just one question. I believe I'm just about on my 15 minutes.

Q Do you remember anything else about the -- anything you did in contributing to the preparation of the patent application that was either filed in the US or the UK relating to the subject matter of the 860 patent?

MS. WIGMORE: You can answer the question of whether you remember, but I instruct you not to reveal the substance of any attorney-client communications.

A I don't recall it anyway. I almost feel like saying I'm sorry I don't recall it, but I don't

recall it.

Q Okay, let's go on our break.

VIDEOGRAPHER: Going off the record, the time is 12.30.

(12.30 pm)

OFF THE RECORD

(1.22 pm)

VIDEOGRAPHER: This marks the beginning of videotape number 2, back on the record, the time is 13.22.

Q Dr. Owen, before the break, you mentioned that Dr. Naylor, you considered him to be an expert on testing for CNS effects, is that correct?

MS. WIGMORE: Objection.

A Bob Naylor and Brenda Costall were and I think still are respected CNS pharmacologists.

Q Can you tell me what your understanding is of their qualifications?

MS. WIGMORE: Can I just clarify, you're talking about at the time that he called them, or at the present time?

Q At the time that you called them.

A Well, they were both academic members of staff in the pharmacy department at the University of Bradford. I could probably make a very informed guess of their qualifications, but I don't absolutely know their qualifications. I am aware and I was aware that they had published extensively in CNS pharmacology.

Q And in your estimation, would both Professor Costall and Professor Naylor be qualified to speak to the subject matter of the 860 patent?

MS. WIGMORE: Objection.

A I don't know, I don't know the answer to that. I don't know, for example, if they have ever seen it. I don't know.

Q But if they were shown it, would they be able to speak to that subject matter?

MS. WIGMORE: Objection, vague.

A Well, I don't know what their competencies are beyond what I've told you as CNS pharmacologists.

Q And some of their work is described in the 860 patent, correct?

A Some of the experiments that they did after I consulted with them are included in the patent, that's correct.

Q When you said you came up with the hypothesis that ropinirole could be used to treat Parkinson's disease, you said that there were two factors that you considered aside from your general knowledge of pharmacology, those being that you knew ropinirole was a selective dopamine agonist on the D2 receptor, and that also you had seen the CNS effects from the experiments that Annette Wright had been conducting, is that accurate?

A I can't remember if I said that in this deposition, but that would be accurate. Whether I've actually said it previously today, I can't remember. It's not -- as you've probably seen, I wish I was feeling a bit more relaxed than I am.

Q Let me ask you this: were you aware at the time that you came up with your hypothesis about ropinirole, were you aware of other compounds that were selective D2 dopamine agonists that exhibited CNS effects but were not effective in treating

Parkinson's disease?

A I don't know the answer to that. I don't remember what I knew at that level of detail at that time.

Q At the time you came up with your hypothesis about the potential use of ropinirole to treat Parkinson's disease, did you think that there were any other compounds that were structurally similar to ropinirole that could be used for that same purpose?

MS. WIGMORE: Objection.

A My focus at that time was entirely on ropinirole, there is one compound and one compound alone that was the subject of a project development program.

Q And you mean ropinirole by that one compound?

A I mean ropinirole, I do embrace in that salts of ropinirole, but one entity, if you will.

Q And ropinirole or its salts, that was the only compound that you discussed with Professor Costall, is that correct?

That doesn't distinguish for me, reading it now, as to whether this was a follow-up to another meeting, or may have reflected the first meeting, it doesn't make that distinction.

Q If you had a prior meeting with -- or conversation with either Professor Naylor or Professor Costall, would you have reported that to this project team?

MS. WIGMORE: Objection.

A I don't know. I mean, I just can't recall that.

Q This excerpt indicates that Professor -- that you were about to ask Professor Naylor about the design of an investigation into the neurobehavioral effects of SK&F 101468A, which you previously identified as ropinirole, correct?

A Yes, correct.

Q Can you tell me what neurobehavioral effects Professor Naylor or anyone else at Bradford was being asked to investigate?

A Well, we come back to the starting point that the reason we went to Costall and Naylor, the

reason I went to Costall and Naylor originally, I subsequently delegated it, was that they were one of a number of groups who could do, as it's written here, neurobehavioral studies, but they were particularly expert in the context of models for Parkinson's disease, and I wanted somebody who could specific -- amongst the choices that might have been available to me, in that I didn't approach others, I can't say they were available, what I wanted -- I selected them because they were best equipped to look at Parkinson models, ergo they were the people best equipped to test the hypothesis that I had taken them -- to them, and confirm whether it was a sound or an unsound hypothesis, not many hypotheses aren't sound, but what was very, very important was to put such studies into context with any other neurobehavioral CNS effects -- I would regard those as almost interchangeable words -- and the reason we went to experts for that broad profile was to allow them to use their expertise and advise me what other studies would be needed to give it that context. I went to experts for their

expertise.

Q And what studies did either Professor Naylor or Professor Costall indicate should be done to determine if ropinirole had these neurobehavioral CNS effects?

A I simply can't remember that detail at this stage, and I'm going to say now, because it will come out, the nature of my -- of activity, I set this up, was the hypothesis that I had developed that was being tested for Parkinson's, but I delegated a lot of the day-to-day activity to others, and in particular to Roger Eden.

Q Other than Mr. Eden, was there anyone else that you delegated the day-to-day contact activity with the Bradford researchers to?

A I can't recall anybody else. There's a distinction between Roger was the guy who reported to me, and therefore he was the only one whom I could delegate. If other folks from other parts for whom I was not responsible talked to them, then they talked to them.

Q Okay, but the first contact between anyone

test the hypothesis, and hence I went to Professor Costall and Professor Naylor.

Q In describing your hypothesis or what you wanted Professor Costall and Professor Naylor to test for, did you focus only on the effectiveness of ropinirole to treat Parkinson's disease, or were you more broadly looking at all CNS effects?

MS. WIGMORE: Objection.

A Well, the way I like to express it is the way I've expressed it now two or three times, we wanted to test the hypothesis for Parkinson's disease, and put it into an overall context by determining whether there were any other effects on the central nervous system.

Q And I believe you said that the reason -- one of the reasons that you contacted Professor Costall and Naylor was because you knew that they had previously done work on a marmoset model that could be used to determine effectiveness in treating Parkinson's activity, is that -- Parkinson's disease, is that correct?

A I'm almost certain it must have been

had tested.

Q But they had tested some other compounds for their effectiveness in treating Parkinson's disease using the tests that are --

A I can't go --

MS. WIGMORE: Objection.

A Sorry.

MS. WIGMORE: Let him finish the question.

A I'm sorry.

MS. WIGMORE: Can you repeat the question so the record's clear?

MR. BRAHMA: Sure.

Q But prior to your first contacting Professor Costall, Professors Costall and Naylor had tested some other compounds for their effectiveness in treating Parkinson's disease using the tests that they ultimately ran with respect to ropinirole, is that accurate?

MS. WIGMORE: Objection.

A I can't recall now what compounds I may or may not have known at that time they tested. But I regarded them as people with models to test

compounds for Parkinson's activity.

Q Let me take a step back. You previously mentioned the two factors that led you to hypothesize that ropinirole might be effective in treating Parkinson's: the selective D2 receptor agonist activity and the observation of CNS effects.

At that point in time, if ropinirole had shown no -- excuse me -- no D2 receptor agonist activity, would you have believed that it would not be effective in treating Parkinson's disease?

MS. WIGMORE: Objection, calls for speculation.

A You just asked me if ropinirole hadn't shown D2 agonist activity, when there was a wealth of information from Philadelphia that it did, so it's a hypothetical question based on a false hypothesis.

Q Well, you found CNS effects when Philadelphia said there were no CNS effects, correct?

A We found CNS effects, and the message was that there weren't CNS effects.

department.

A Insofar as I can't remember the detail of the interaction, all I can say is I don't remember.

Q Okay. If one of the other compounds in that general structural formula had been found to have no D2 agonist activity, would you then conclude that it would not be effective in treating Parkinson's disease?

MS. WIGMORE: Objection.

A I have no basis to speculate one way or the other.

Q And you're saying that based on your knowledge today, or based on your knowledge at the time that you drafted this patent -- at the time the patent application for the 860 patent was prepared?

MS. WIGMORE: Objection.

A I don't recall what happened in detail at that time, therefore I'm unable to answer that question. As of today, by implication, it's the best part of 20 years since I did active pharmacology; anything what I knew, I only know less now.

judgment for the patent department.

Q But you reviewed --

A Not a pharmacologist making pharmacological judgments.

Q But you reviewed this patent application before it was submitted, correct?

A Yes, I'm sure I reviewed it.

Q And when you reviewed it, you said that you were the first and sole inventor of the subject matter that's claimed in this patent, correct?

A That was signed on the piece of paper, yes.

Q But I believe what you said now is that although there are a number of compounds that are described and claimed in this patent, you only developed a hypothesis as to one specific compound, and that's ropinirole, was that accurate?

A That is absolutely what I've said all the way through, and that is accurate.

Q And my question then to you is: based on the information you had about ropinirole, would it be -- would that information be sufficient to draw

a hypothesis as to whether these other compounds within that general structure would be effective in treating Parkinson's disease?

MS. WIGMORE: Objection.

A It is a matter for the legal department to determine how broadly they then choose to draft the patent. They drafted it, I didn't draft it, I'm very comfortable that they are very expert in the drafting of patents, so I have tried to tell you as reliably as I can what I did, and this is what the legal department did by way of drafting arising from that.

Q And that general structural formula in column 2 of the 860 patent, that's not something that you came up with, correct?

A Oh, very definitely correct.

Q So as far as you know, it's possible that there are compounds covered by that general structural formula that have absolutely no effectiveness in treating Parkinson's disease, is that accurate?

MS. WIGMORE: Objection.

tests, I went to the CNS experts.

If they say to me, "These are good tests to test your hypothesis", my inclination, my inclination at that time is to believe them, and therefore they conducted those tests, but I happily deferred to their expertise to know which tests would be appropriate to evaluate what was my hypothesis.

Q Okay, and just to be clear, at the time they were conducting these tests, they were not only looking for effectiveness in treating Parkinson's, but also other CNS effects, correct?

A What I recall was going to them because I -- they were the selected place, they were the rational place to select as well, people to test the Parkinson's hypothesis, but it's no good looking at Parkinson's in isolation of any other effects the compound may have on the central nervous system, it's what -- what I referred to as putting the Parkinson's effects into context with other CNS activity.

Q So not all these tests would necessarily

you believe this is a peer reviewed journal article, correct?

A It is normal for things published in the Journal of Medicinal Chemistry to be peer reviewed, yes.

Q Do you know what the backgrounds would have been of the people who would have reviewed this paper?

MS. WIGMORE: Objection.

A I have absolutely no basis to know what their background is.

Q Would this paper have necessarily been reviewed by CNS pharmacologists?

A That would be entirely a matter for the editor, and I don't know who the editor is, nor what would have influenced the decision.

Q Let me go up a little bit, I'm looking at your patent again, exhibit 17, we were previously looking at column 1, the paragraph starting at line 54, I'm going to ask you to go to the paragraph above that, which says:

"It has now been found that certain

indolone derivatives, known in the art as presynaptic D2 agonists, having utility as cardiovascular agents [and then it cites a European patent] also are postsynaptic D2 agonists in the brain and hence are expected to have utility in the treatment of Parkinson's."

Do you see that?

A Yes, I do.

Q Is that an accurate assessment of what you hypothesized when you first spoke to -- before you first spoke to Dr. Costall?

A That's an accurate reflection of what would be appropriate if the hypothesis was correct, but if you're asking -- I need to be sure what you're asking me, because that's not the language I would have used with Professor Costall.

Q At the time you first came up with the hypothesis that ropinirole could be used to treat Parkinson's disease, were you aware of this distinction between presynaptic and postsynaptic D2 agonists?

A I understand the concepts of presynaptic

D2 and postsynaptic D2 receptors, it's the receptors that are crucial, the agonist is an agonist at D2 receptors, regardless of whether they're pre or postsynaptic.

Q Let me see if I understand that correctly.

A It's a point of pharmacology obviously.

Q So a compound will be a D2 receptor agonist regardless of whether the receptor is presynaptic or postsynaptic?

MS. WIGMORE: Objection. Go ahead.

A If it's an agonist for D2 receptors, it will be an agonist for D2 receptors, and whether they are presynaptic or postsynaptic is a piece of anatomy, not a piece of pharmacology.

Q So you would expect a compound that was a D2 agonist at a presynaptic D2 receptor to also be a D2 agonist at a postsynaptic D2 receptor?

MS. WIGMORE: Objection.

A If a compound is a D2 agonist, I would expect it to be a D2 agonist at D2 receptors regardless of their anatomical location.

Q And was that your understanding at the

time you first came up with the hypothesis that ropinirole could be used to treat Parkinson's disease?

A My hypothesis was that the D2 agonist, as represented by ropinirole, it was ropinirole data that I had, the hypothesis was that it could be an anti-Parkinson's drug. It wasn't necessary, nor did I, to the best of my memory, make any statements about the significance of pre or postsynaptic location of the receptors, in order to -- that wasn't necessary, in order to be a part of the hypothesis.

Q So you knew that it was -- that ropinirole was a D2 agonist, to you it didn't matter whether it had an effect on presynaptic D2 receptors or postsynaptic D2 receptors, in order to be effective for Parkinson's disease?

MS. WIGMORE: Objection.

A In order to be effective in Parkinson's disease, the evidence that we have now is that it is an agonist at postsynaptic receptors, but this -- whether it's pre or postsynaptic, in my view, is

an absolute irrelevance. A D2 agonist is a D2 agonist for D2 receptors regardless of their location.

Q Let me draw your attention a little bit further up in column 1, the paragraph that starts at approximately line 35 says:

"An alternative form of therapy is to administer postsynaptic dopamine agonists, for example, ergot alkaloids such as bromocriptine."

Do you see that?

A I do.

Q When it's talking about an alternative form of therapy, you're referring to therapy to treat Parkinson's disease, right?

A I'm sure that is what is intended, because I'm reading it, and it doesn't say so, does it? But I'm sure that's what's intended.

Q And are you familiar with the compound bromocriptine?

A I had some familiarity with bromocriptine at that time.

MS. WIGMORE: Objection.

A And I'm telling you I don't remember whether I might have done so on another occasion.

Q So you don't specifically remember whether you ever communicated information about your invention to anyone from the patent department at GSK?

A I can't remember, there's nothing in my head that says, "I remember that occasion when I did so". It's quite different to saying it did or didn't happen, I'm saying I can't remember an occasion when it happened.

I have recall in a very broad and general sense of occasions when I went on the floor where the patent department was, but I can't tell you that I remember any discussion with them, and because I was responsible for things other than just this program, when I was there, I can't tell you what topic I may have discussed with them. I'm sure it would help us both if I could, but I can't, sorry.

MS. WIGMORE: Nevertheless, I would

when it's administered to a patient with Parkinson's disease, correct?

MS. WIGMORE: Objection.

A I wouldn't expect there to be any evidence of anti-Parkinson activity, because based on my knowledge, which may be limited, because I'm not a clinician, I don't know how you could measure anti-Parkinson activity.

Q In a healthy patient?

A In a healthy patient, so the statement could be accurate, but one could wonder why on earth it's been written.

Q And again, your assumption there that this test was done in healthy volunteers, what is that based on?

A Because the normal way to start studies is in healthy volunteers, so I agree that that's a supposition, but it's a very reasonable supposition.

Q Can you tell me what your educational background is?

A My educational background, after leaving

school, I did a bachelors degree in pharmacy at the College of Technology in Brighton. I started a PhD at the same institution, but shortly after starting, my supervisor moved to the University of Aston, which is in Birmingham, and I completed my PhD at Aston.

Q And in what area was your PhD?

A The title of my PhD was "The interaction between angiotensin and the sympathetic nervous system". It was a -- that means I did a cardiovascular PhD.

Q You previously said that you didn't consider yourself to be an expert with respect to CNS pharmacology. Did you study CNS pharmacology as part of either your bachelors or doctorate work?

A We did a very small amount of work -- as a pharmacist, one looked at things from the perspective of drugs which may at that stage have been marketed, you know, the pharmacist might deal with that were CNS drugs, so I'm sure I did that course, because that's going back another 20 years beyond this, so that I would have done it is a fact.

I can't, for example, remember we had an exam question in finals on anaesthetics. In my PhD, I did not do any studies of CNS.

Q And you wouldn't consider your coursework to give you enough background in CNS pharmacology --

A I certainly would not --

MS. WIGMORE: Wait for the question to be asked.

A Sorry.

Q Let me repeat it. You wouldn't consider your coursework to give you enough of a background in CNS pharmacology to make you an expert in that area?

A Oh no, I've never been an expert in that area, sorry.

Q Have you worked with other compounds -- well, let me back up a step. Once you finished your PhD, did you start working?

A Yes, I did start working on completion of my PhD, I worked for Sando in Basle in Switzerland.

Q And how long were you at Sandos?

A I went there, gosh, September or October?